



11) Publication number:

0 448 029 A3

(12)

## **EUROPEAN PATENT APPLICATION**

(21) Application number: 91104207.5

(51) Int. Cl.5: **A61K** 31/35

② Date of filing: 19.03.91

3 Priority: 23.03.90 JP 72022/90

23.03.90 JP 72023/90 12.06.90 JP 151552/90 15.06.90 JP 155108/90

43 Date of publication of application:

25.09.91 Bulletin 91/39

84 Designated Contracting States:

DE FR GB IT

Bate of deferred publication of the search report:

10.06.92 Bulletin 92/24

(1) Applicant: NIPPON KAYAKU KABUSHIKI

**KAISHA** 

11-2, Fujimi 1-chome Chiyoda-ku

Tokyo 102(JP)

2 Inventor: Hosono, Makoto

46, Honcho-8-chome Kitamoto-shi(JP) Inventor: Fujita, Akira

683-1, Mihashi-1-chome

Omiya-shi(JP)

Inventor: Izumi, Giichi

33-16, Daizawa-5-chome, Stagaya-ku

Tokyo(JP)

Inventor: Tatee, Tochiro

18-8, Nakajujo-1-chome, Kita-ku

Tokyo(JP)

Inventor: Takahira, Takashi

1090, Kamiochiai Yono-shi(JP)

Inventor: Furuta, Yasuhiko

1-37, Fujimi-2-chome, Fukiagemachi

Kitaadachi-gun, Saitama-ken(JP)

Inventor: Sakai, Michiko

58-2-5003, Akabene-1-chome

Kita-ku, Tokyo(JP)

Inventor: Ishizuka, Osamu

17-10, Simo-3-chome

Kita-ku, Tokyo(JP)

Inventor: Terada, Takashi

16-10, Hibarino-1-chome

Konosu-shi(JP)

Inventor: Itoh, Junpei

1090-B212, Kamiochiai

Yono-shi(JP)

(74) Representative: Türk, Gille, Hrabal

**Brucknerstrasse 20** 

W-4000 Düsseldorf 13(DE)

Movel pharmaceutical uses of forskolin derivatives.

The present invention relates to a platelet aggregation inhibiting or controlling agent, spasmolytic agent, therapeutic agent for skin ulcer, peripheral circulation improving agent for limbs and differentiation inducing and promoting agent which contain as active principle a forskolin derivative represented by the formula (I):

EP 0 448 029 A3

wherein R1 is a group represented by the formula

$$-CO \leftarrow CH_2 \rightarrow \frac{R^4}{n} N-R^3$$

(wherein R³ and R⁴ are each hydrogen or lower alkyl group, or R³ and R⁴ may be combined to represent lower alkylene group which may have oxygen or nitrogen atom in the linking chain, and n is an integer of 1 to 5); R² represents hydrocarbon group having 2 to 3 carbon atoms; and Ac represents acetyl group, or a physiologically acceptable salt thereof.



## **EUROPEAN SEARCH REPORT**

EP 91 10 4207

		DERED TO BE RELEVAL dication, where appropriate,	Relevant	CI ASSIEICATION OF THE
Category	of relevant pa		to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	May 1982, pages 680 al.: "Inhibition of stimulation of cycl	OGY, vol. 31, no. 3, -687; A.M. SIEGL et aggregation and ic AMP generation in ets by the diterpene	1-3	A 61 K 31/35
	NAUNYN-SCHMIEDEBERG PHARMACOLOGY, vol.: pages 119-121, Sprin KARIYA et al.: "Efformation designed to the second designed at generation" * Whole article *	331, no. 1, 1985, nger-Verlag; T. ect of forskolin on	1-3	
	MEDICINAL RESEARCH   2, April-June 1983, Wiley & Sons Inc.;   al.: "Forskolin: A with antihypertensive inotropic, platelet inhibitory, and aderactivating properties * Whole article, espansive in the serious of the se	labdane diterpenoid ve, positive aggregation nylate cyclase es" bec. pages	1-3	TECHNICAL FIELDS SEARCHED (Int. Cl.5)
	BIOCHEMICAL PHARMACC 24, 1982, pages 4071 Press Ltd., GB; S. A "Forskolin (a powerf human platelet aggre * Whole article * 	L-4074, Pergamon ADNOT et al.: ful inhibitor of	1-3	
	The present search report has be	en drawn up for all claims	_	
	Place of search	Date of completion of the search	<del></del>	Examiner
THE HAGUE		05-12-1991	GAC	
CATEGORY OF CITED DOCUMENTS  X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document		E : earlier patent de after the filing her D : document cited L : document cited	ocument, but publ date in the application for other reasons	ished on, or

EPO FORM 1503 03.82 (P0401)



	CL	AIMS INCURRING FEES
The	oresen	t European patent application comprised at the time of filling more than ten claims.
[		All claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for all claims.
[		Only part of the claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid,
_		namely claims:
Ĺ		No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.
	LA	CK OF UNITY OF INVENTION
The S		Division considers that the present European patent application does not comply with the requirement of unity of
inven name	tion an	d relates to several inventions or groups of inventions,
Hastie	ıy.	
	see	sheet -B-
	]	All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
	]	Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid,
		namely claims:
	¥	None of the further search fees has been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.
		namely claims: 1 – 3



## EUROPEAN SEARCH REPORT

Application Number

EP 91 10 4207

ategory	Citation of document with indicati of relevant passages	on, where appropriate,	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	MOLECULAR PHARMACOLOGY, 1987, pages 133-139; A. al.: "Stimulation of acby water-soluble analog forskolin"  * Whole article *	1-3	ATTACATION (III. C. 3)	
				TECHNICAL FIELDS SEARCHED (Int. Cl.5)
	The present scarch report has been dra	•	_	
<b></b> -	Place of search	Date of completion of the search		Examiner
C X : parti Y : parti docu A : techi	HAGUE  ATEGORY OF CITED DOCUMENTS  cularly relevant if taken alone cularly relevant if combined with another ment of the same category nological background written disclosure	E : earlier patent d after the filing D : document cited L : document cited	date in the application for other reasons	nvention hed on, or



## LACK OF UNITY OF INVENTION a priori

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions.

namely:

- 1. Claims 1-3: Use of a forskolin derivative of the formula of claim 1 in the manufacture of a medicament for treating a disease caused by platelet aggregation.
  - Claims 4-6: Use of a forskolin derivative of the formula of claim 1 in the manufacture of a medicament for treating skin ulcer.
  - 3. Claims 7-8: Use of a forskolin derivative of the formula of claim 1 in the manufacture of a medicament for treating vasospasm.
  - 4. Claims 9-10: Use of a forskolin derivative of the formula of claim 1 in the manufacture of a medicament for treating a disease caused by undifferentiated cells.
  - 5. Claims 11-13: Use of a forskolin derivative of the formula of claim 1 in the manufacture of a medicament for treating a disease caused by trouble in peripheral blood circulation in limbs.